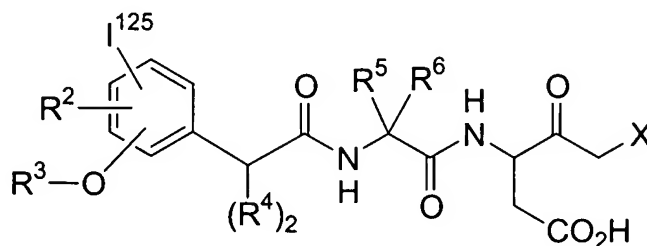


Amendments to the Claims:

This listing of claims replaces all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (original) A compound represented by Formula I:



I

or a salt, ester or hydrate thereof, wherein:

X is halo, or

X is -O-W-Z, wherein W is a bond, -CH₂-, -C(O)- or -C(O)CH₂-;

Z is selected from the group consisting of:

- (1) H,
- (2) C₁-₁₁alkyl,
- (3) C₃-₁₁cycloalkyl or a benzofused analog thereof,
- (4) phenyl or naphthyl, and
- (5) HET¹, wherein HET¹ represents a 5- to 10-membered mono- or bicyclic,

aromatic or non-aromatic ring, or a benzofused analog thereof, containing 1-3 heteroatoms selected from O, S and N,

groups (2), (3) and (5) above are optionally substituted with 1-2 oxo groups,

groups (2) – (5) above are further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo
- (b) nitro,
- (c) hydroxy,
- (d) C₁₋₄alkyl,
- (e) C₁₋₄alkoxy,
- (f) C₁₋₄alkylthio,
- (g) C₃₋₆cycloalkyl,
- (h) phenyl or naphthyl,
- (i) phenoxy,
- (j) benzyl,
- (k) benzyloxy, and
- (l) a 5 or 6-membered aromatic or non-aromatic ring containing from

1-3 heteroatoms selected from O, S and N,

groups (d)-(g) above are optionally substituted with oxo and 1-3 substituents independently selected from halo and C₁₋₄alkoxy,

groups (h) – (l) above are optionally substituted with 1-3 substituents independently selected from halo and C₁₋₄alkyl, and

group (4) is further optionally substituted up to its maximum with halo groups;

R² is selected from the group consisting of:

- (1) H,
- (2) halo,
- (3) hydroxy,
- (4) nitro,
- (5) cyano,
- (6) C₁₋₁₀alkyl, C₃₋₁₀cycloalkyl, C₁₋₁₀alkoxy, –S(O)₀₋₂C₁₋₁₀alkyl or

–NHC₁₋₁₀alkyl, each optionally substituted with 1-2 oxo or carboxy groups and further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo,
- (b) hydroxy
- (c) cyano,
- (d) C₁₋₄alkoxy,
- (e) -NHR⁷, wherein R⁷ is independently H or C₁₋₅alkyl,
- (f) -S(O)₀₋₂C₁₋₄alkyl, and
- (g) HET², wherein HET² represents a 5- to 7-membered aromatic or

non-aromatic ring containing 1-4 heteroatoms selected from O, S and NR⁸, wherein R⁸ is independently H or C₁₋₅alkyl, said HET² being optionally substituted with oxo and further optionally substituted with 1-2 substituents independently selected from halo and C₁₋₄alkyl, said C₁₋₄alkyl being optionally substituted with 1-3 halo groups,

- (7) phenoxy or -S(O)₀₋₂phenyl,
- (8) benzyloxy or -S(O)₀₋₂benzyl,
- (9) benzoyl,
- (10) phenyl or naphthyl,
- (11) -O-HET² or -S-HET², said HET² being optionally substituted with oxo

and further optionally substituted as defined below, and

(12) HET³, wherein HET³ is a 5- or 6-membered aromatic or non-aromatic ring, or a benzofused analog thereof, containing from 1 to 4 heteroatoms selected from O, S and N, said HET³ being optionally substituted with oxo and further optionally substituted as defined below,

groups (7) - (12) above are each optionally substituted with 1-2 substituents independently selected from the group consisting of: halo, cyano, C₁₋₄alkyl and C₁₋₄alkoxy, said C₁₋₄alkyl and C₁₋₄alkoxy being optionally substituted with 1-3 halo groups;

R³ is phenyl or C₁₋₁₀alkyl, said C₁₋₁₀alkyl optionally substituted with 1-2 oxo or carboxy groups and further optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo,
- (b) hydroxy
- (c) cyano,
- (d) C₁₋₄alkoxy,

(e) -NHR^7 , wherein R^7 is independently H or C_{1-5} alkyl,
(f) $\text{-S(O)}_{0-2}\text{C}_{1-4}$ alkyl, and
(g) HET^2 , wherein HET^2 represents a 5- to 7-membered aromatic or non-aromatic ring containing 1-4 heteroatoms selected from O, S and NR^8 , wherein R^8 is independently H or C_{1-5} alkyl, said HET^2 being optionally substituted with oxo and further optionally substituted with 1-2 substituents independently selected from halo or C_{1-4} alkyl, said C_{1-4} alkyl being optionally substituted with 1-3 halo groups,

each R^4 is independently selected from the group consisting of: H, halo, hydroxy, C_{1-6} alkyl and C_{1-4} alkoxy, said C_{1-6} alkyl and C_{1-4} alkoxy being optionally substituted with oxo and further optionally substituted with 1-3 halo groups; and

R^5 is selected from the group consisting of: H, phenyl, naphthyl, C_{1-6} alkyl optionally substituted with OR^{12} and 1-3 halo groups, and C_{5-7} cycloalkyl optionally containing one heteroatom selected from O, S and NR^{13} ,

wherein R^{12} is selected from the group consisting of: H, C_{1-5} alkyl optionally substituted with 1-3 halo groups, and benzyl optionally substituted with 1-3 substituents independently selected from halo, C_{1-4} alkyl and C_{1-4} alkoxy, and

R^{13} is H or C_{1-4} alkyl optionally substituted with 1-3 halo groups; and

R^6 represents H;

or in the alternative, R^5 and R^6 are taken in combination and represent a ring of 4-7 members, said ring optionally containing one heteroatom selected from O, S and NR^{13} .

2. (original) The compound according to Claim 1 wherein X is halo.

3. (original) The compound according to Claim 1 wherein X is -O-W-Z .

4. (original) The compound according to Claim 3 wherein Z is selected from the group consisting of:

- (1) C₁₋₁₁alkyl,
- (2) C₃₋₁₁cycloalkyl or a benzofused analog thereof, and
- (3) phenyl or naphthyl,

wherein groups (1) – (3) above are optionally substituted with 1-3 substituents independently selected from the group consisting of:

- (a) halo
- (b) nitro,
- (c) hydroxy,
- (d) C₁₋₄alkyl,
- (e) C₁₋₄alkoxy,
- (f) C₁₋₄alkylthio,
- (g) C₃₋₆cycloalkyl,
- (h) phenyl or naphthyl,
- (i) phenoxy,
- (j) benzyl and
- (k) benzyloxy.

5. (original) The compound according to Claim 1 wherein R³ is methyl.

6. (original) The compound according to claim 1 wherein R² and each R⁴ are hydrogen.

7. (original) The compound according to claim 1 wherein R⁵ is selected from the group consisting of: C₁₋₆alkyl, phenyl and naphthyl.

8. (original) The compound according to claim 1 wherein:

X is halo or –O–W–Z;

W is a bond, –CH₂–, –C(O)– or –C(O)CH₂–;

Z is selected from the group consisting of:

- (1) C₁₋₆alkyl, optionally substituted with 1-3 halo groups,
- (2) C₃₋₁₁cycloalkyl or a benzofused analog thereof, and
- (3) phenyl or naphthyl, optionally substituted with 1-3 groups independently selected from halo or C₁₋₄alkyl,

R³ is methyl, ethyl or phenyl;

R² and each R⁴ are hydrogen;

R⁵ is selected from the group consisting of: C₁₋₆alkyl, ~~C₅₋₇cycloalkyl~~ C₅₋₇cycloalkyl, phenyl and naphthyl; and

R⁶ is hydrogen.

9 to 11. (canceled)

12. (withdrawn) A method for detecting active caspase-3 in cells or tissues of a mammal comprising contacting said cells or tissues with a compound of Claim 1 and detecting active caspase-3.

13. (canceled)

14. (withdrawn) A method for determining the caspase-3 active site occupancy of a sample reversible caspase-3 inhibitor in an animal model of cellular injury comprising:

- 1) administering to said animal said sample reversible caspase-3 inhibitor;
- 2) euthanizing said animal and extracting said injured cells;
- 3) contacting said injured cells *ex vivo* with a compound according to Claim 1;
- 4) detecting the amount of said compound to determine the number of caspase-3 free active sites; and

5) comparing said number of caspase-3 free active sites to the total measure of active caspases to determine the caspase-3 active site occupancy.

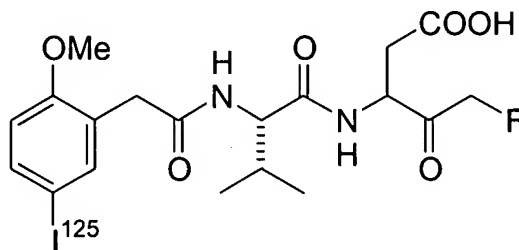
15. (withdrawn) A method for determining the caspase-3 active site occupancy of a sample reversible caspase-3 inhibitor in a cell culture comprising:

- 1) contacting said cell culture with a sample reversible caspase-3 inhibitor;
- 2) contacting said cell culture with a compound according to Claim 1;
- 3) detecting the amount of said compound to determine the number of caspase-3 free active sites; and
- 4) comparing said number of caspase-3 free active sites to the total measure of active caspases to determine the caspase-3 active site occupancy.

16. (withdrawn) A kit for detecting active caspase-3 in cells or tissues of a mammal comprising a compound of Claim 1.

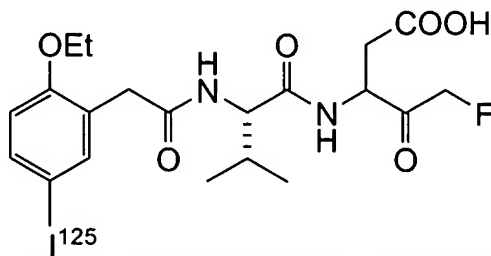
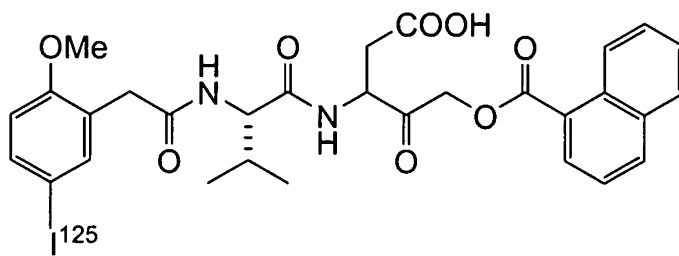
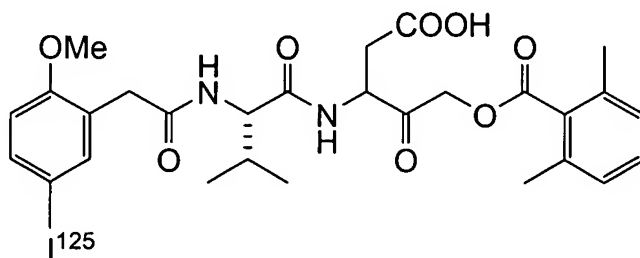
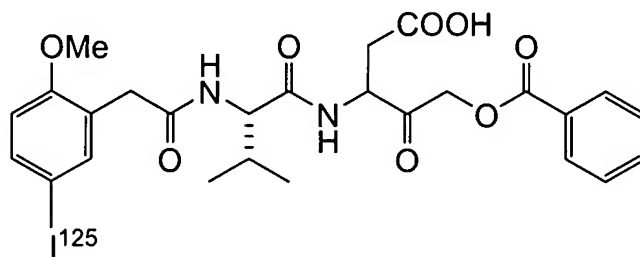
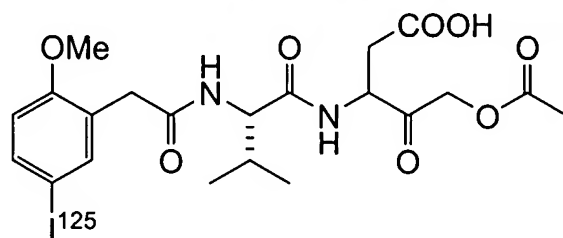
17. (canceled)

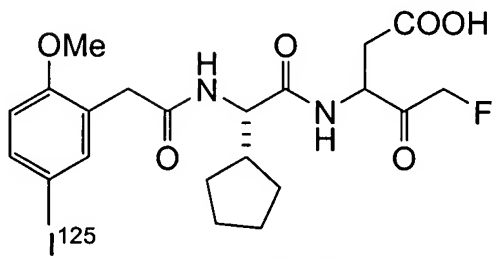
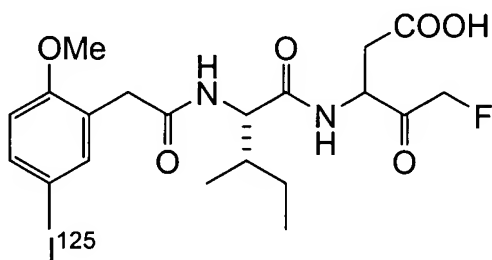
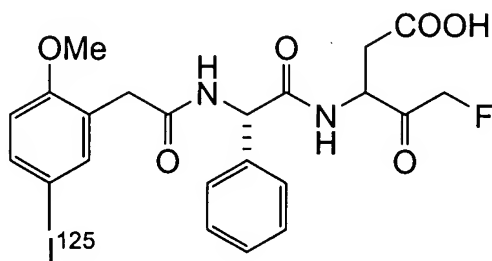
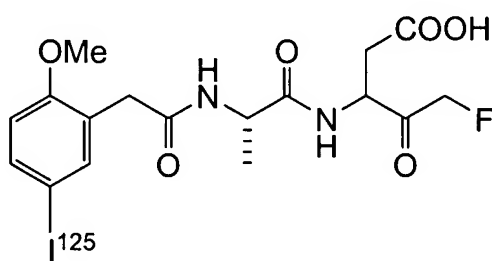
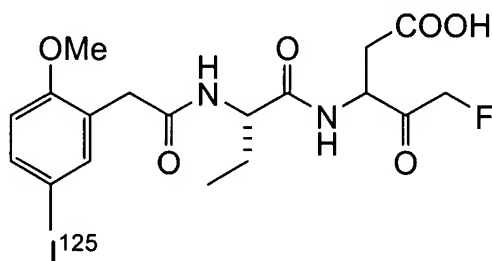
18. (original) The compound according to Claim 1 which is

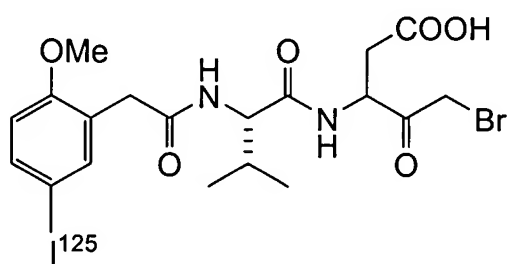
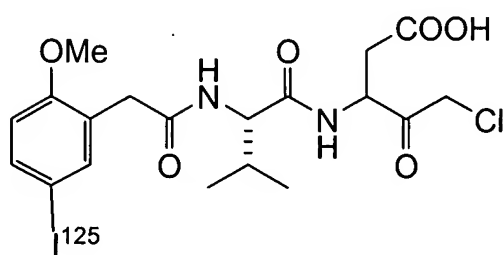
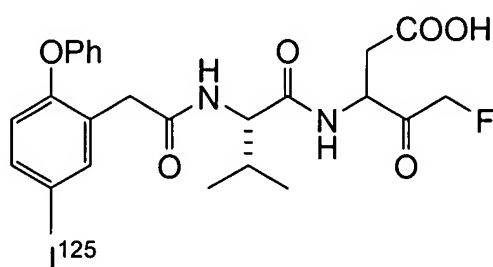
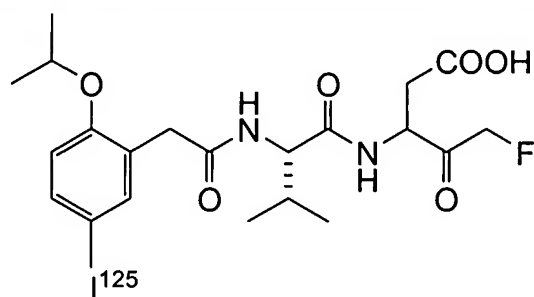


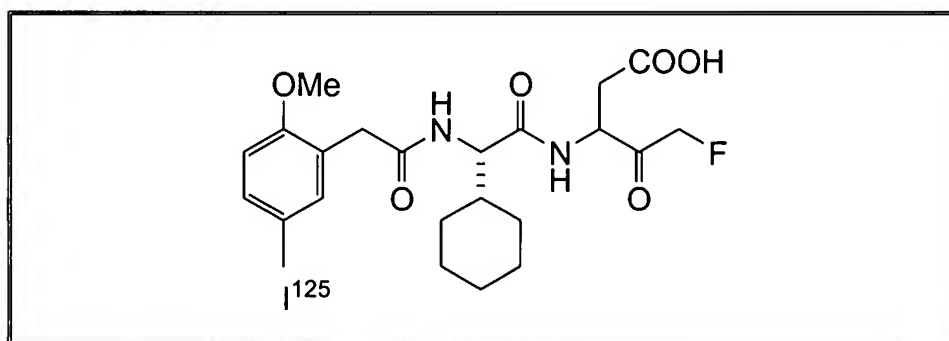
or a salt, ester or hydrate thereof.

19. (original) A compound according to Claim 1 which is selected from the following table:









or a salt, ester or hydrate of any of the above.

20. (withdrawn) A compound of any one of claims 1 to ~~14~~ 8, 18 or 19 for use in detecting active caspase-3 in cells or tissues of a mammal.

21. (withdrawn) A compound of any one of claims 1 to ~~14~~ 8, 18 or 19 for use in determining the capsase-3 active site occupancy of a sample reversible caspase-3 inhibitor in an animal model of cellular injury.